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10/580,547	04/13/2007	Ge Ming Lui	266575	5979

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EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/580,547	LUI, GE MING	
	Examiner	Art Unit	
	SHERIDAN R. MACAULEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *10-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are pending.

Election/Restrictions

1. Applicant's election without traverse of claims 1-9 in the reply filed on November 13, 2009 is acknowledged. The reply is deemed proper and is therefore made final.

2. Claims 10-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Claims 1-9 are examined on the merits in this Office action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 and its dependents are rendered indefinite by the recitation of "the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer or a mammal" in lines 3-4 of the claim. It is unclear whether applicant intends for this to mean that the cells may be derived from the area of the brain of a mammal, derived from the epithelium layer, or derived from a mammal in general; or whether applicant

intends to claim that the cells are derived from "the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer of a mammal". Appropriate correction to clarify this matter is required.

7. Claim 4 is rendered indefinite by the recitation of “said attachment proteins can be laminin, fibronectin and RGDS.” It is unclear whether applicant intends for the attachment proteins to be selected from the group consisting of the recited proteins, whether applicant intends for all of the proteins to be present in the composition or whether the recited proteins are merely exemplary. If applicant intends the former, it is recommended that the language be amended to “selected from the group consisting of..." or some other appropriate alternative.

8. Claim 5 is rendered indefinite by the recitation of “cells are mixed with the polymer gel solution (10 to 20% W/V). It is unclear whether applicant intends for the cells to be present in the solution at 10 to 20% W/V, for the polymer gel to be in solution at 10 to 20% W/V, or some other alternative. Applicant is also advised that the term "W/V" is not clearly set forth in the claim. The term should be corrected to “weight per volume", "weight/volume” or the appropriate meaning term applicant intends for the term.

9. Claim 6 is rendered indefinite by the recitation of "wherein the concentration of live pigmented cells is at least 200,000 cells to about 800,000 cells." It is unclear how much of the composition this amount of cells is intended to be present in. For instance, the composition could comprise 200,000 cells per microgram, per milliliter or per square meter.

10. Claim 9 is rendered indefinite by the recitation of "a water soluble comprising a poly-vinyl alcohol." It is unclear whether applicant intends to claim that the composition comprises a water soluble poly-vinyl alcohol, a water soluble agent comprising a poly-vinyl alcohol, or some other alternative.

11. Therefore, the metes and bounds of the claims would be unclear to one of ordinary skill in the art.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Biomedical Microdevices 4:257-266; document cited in IDS) in view of Subramanian (Seminars in Neurology, 1, 103-115; document cited in IDS). The claims recite a composition useful for the prevention, inhibition or treatment Parkinson's

disease in a mammal comprising: a) live pigmented cells derived from the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer or a mammal; and b) a biodegradable polymer gel capable of photo-induced cross linking. The claims further recite that said biodegradable polymer gel further comprises a water soluble macromer having poly(ethylene glycol)di-ethylphosphatidyl(ethylene glycol)methacrylate, or attachment proteins and growth factors to enhance the survival of pigmented cells after implantation, wherein said attachment proteins can be laminin, fibronectin, and RGDS. The claims further recite that the live pigmented cells are mixed with the polymer gel solution (10 to 20% W/V) and that the concentration of live pigmented cells is at least 200,000 cells to about 800,000 cells.

15. Liu teaches compositions comprising live cells and a biodegradable, photopolymerizable polymer gel and that the compositions can be used with many cell types for the delivery of cells to patients (abstract). The reference teaches that the gel may comprise the macromer reicited in the claims (poly(ethylene glycol) diacrylate as well as higher molecular weight polymers; p. 258, par. 3, p. 266, par. 2) and that adhesion peptides (i.e. attachment proteins) may be included in the compositions to enhance viability (p. 266, par. 3).

16. Subramanian teaches that the delivery of live, pigmented retinal cells to a patient was known at the time of the invention for the treatment of Parkinson's disease (abstract). One would have been motivated to combine the compositions of Liu with the cells of Subramanian because Liu is directed to improving cell survival for transplanted cells and Subramanian teaches that strategies to improve cell survival for

transplantation should be used (see abstracts of both references); one would therefore have recognized that the strategies of Liu could have been employed with a reasonable expectation of success in a composition comprising the cell types described by Subramanian. One of ordinary skill in the art would therefore have been motivated to combine the teachings of Subramanian and Liu to arrive at the claimed invention.

17. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Biomedical Microdevices 4:257-266; document cited in IDS) in view of Young (WO 03/018040 A1). The claims recite a composition useful for the prevention, inhibition or treatment Parkinson's disease in a mammal comprising: a) live pigmented cells derived from the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer or a mammal; and b) a biodegradable polymer gel capable of photo-induced cross linking. The claims further recite that said biodegradable polymer gel further comprises a water soluble macromer having poly(ethylene glycol)di-ethylphosphatidyl(ethylene glycol)methacrylate, or attachment proteins and growth factors to enhance the survival of pigmented cells after implantation, wherein said attachment proteins can be laminin, fibronectin, and RGDS. The claims further recite that the live pigmented cells are mixed with the polymer gel solution (10 to 20% W/V) and that the concentration of live pigmented cells is at least 200,000 cells to about 800,000 cells. The claims further recite that said growth factors are bFGF an EGF.

18. Liu teaches compositions comprising live cells and a biodegradable, photopolymerizable polymer gel and that the compositions can be used with many cell

types for the delivery of cells to patients (abstract). The reference teaches that the gel may comprise the macromer recited in the claims (poly(ethylene glycol) diacrylate as well as higher molecular weight polymers; p. 258, par. 3, p. 266, par. 2) and that adhesion peptides (i.e. attachment proteins) may be included in the compositions to enhance viability (p. 266, par. 3).

19. Young teaches compositions comprising retinal pigmented epithelial cells, a biodegradable polymer and growth factors, such as EGF and bFGF (abstract, p. 21, lines 1-19, p. 26, lines 5-15). The reference teaches that the polymer may be replaced with others types of polymer, such as a hydrogel (p. 21, line 35-p. 22, line 3). One would have been motivated to combine the compositions of Liu and Young because Liu is directed to improving cell survival for transplanted cells and Young teaches that cell survival in transplantation is essential and teaches compositions for improvised cell survival. (see abstracts of both references); one would therefore have recognized that the strategies of Liu could have been employed with a reasonable expectation of success in a composition comprising the cell types described by Young. Furthermore, Young teaches that a hydrogel may be used and Liu teaches an improved hydrogel for cell transplants; one would thus have been motivated to combine the teachings to arrive at the claimed invention and could have done so with a reasonable expectation of success. One of ordinary skill in the art would therefore have been motivated to combine the teachings of Young and Liu to arrive at the claimed invention.

20. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Biomedical Microdevices 4:257-266; document cited in IDS) in view of Young (WO 03/018040 A1) as applied to claims 1-7 above, and further in view of Calias et al. (US 6,749,865). The claims recite a composition useful for the prevention, inhibition or treatment Parkinson's disease in a mammal comprising: a) live pigmented cells derived from the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer or a mammal; and b) a biodegradable polymer gel capable of photo-induced cross linking. The claims further recite that said biodegradable polymer gel further comprises a water soluble macromer having poly(ethylene glycol)di-ethylphosphatidyl(ethylene glycol)methacrylate, or attachment proteins and growth factors to enhance the survival of pigmented cells after implantation, wherein said attachment proteins can be laminin, fibronectin, and RGDS. The claims further recite that the live pigmented cells are mixed with the polymer gel solution (10 to 20% W/V) and that the concentration of live pigmented cells is at least 200,000 cells to about 800,000 cells. The claims further recite that said growth factors are bFGF and EGF and that the growth factors are conjugated to polycarbophyll.

21. The teachings of Young and Liu are discussed above. As discussed above, it would have been obvious to combine the references to arrive at nearly all elements of the claimed invention. Neither reference, however, teaches the use of growth factors that are conjugated to polycarbophyll.

22. Calius teaches biologically active conjugates comprising a biopolymer (such as polycarbophil) and a therapeutic agent (such as a growth factor; abstract, col. 3, line 64-

col. 4, line 19, col. 4, lines 49-67). The reference teaches that the conjugates are useful for drug delivery to specific cell and tissue types (col. 2, lines 12-20). One of ordinary skill in the art would have been motivated to use a conjugate for specific targeting to a cell type because the teachings of Young and Liu are directed to compositions comprising a cell-hydrogen matrix for tissue engineering (see, for example, Liu, p. 257, col. 1-p. 258, col. 2). One would therefore recognize that the growth factors necessary to direct the growth of cells in these engineered matrices could be specifically targeted using the teachings of Calius. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings to arrive at the claimed invention because the cells of Young are known to be compatible with hydrogels, such as those taught by Liu, and with growth factors, such as those taught by Young and Calius. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

23. Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Biomedical Microdevices 4:257-266; document cited in IDS) in view of Young (WO 03/018040 A1) as applied to claims 1-7 above, and further in view of Frondoza et al. (US 2001/0014475). The claims recite a composition useful for the prevention, inhibition or treatment Parkinson's disease in a mammal comprising: a) live pigmented cells derived from the substantia nigra area of the brain of a mammal or the retinal pigmented epithelium layer or a mammal; and b) a biodegradable polymer gel capable of photo-induced cross linking. The claims further recite that said biodegradable

polymer gel further comprises a water soluble macromer having poly(ethylene glycol)di-ethylphosphatidyl(ethylene glycol)methacrylate, or attachment proteins and growth factors to enhance the survival of pigmented cells after implantation, wherein said attachment proteins can be laminin, fibronectin, and RGDS. The claims further recite that the live pigmented cells are mixed with the polymer gel solution (10 to 20% W/V) and that the concentration of live pigmented cells is at least 200,000 cells to about 800,000 cells. The claims further recite that said growth factors are bFGF and EGF. The claims further recite that the biodegradable polymer gel further comprises a water soluble comprising a poly-vinyl alcohol.

24. The teachings of Young and Liu are discussed above. As discussed above, it would have been obvious to combine the references to arrive at nearly all elements of the claimed invention. Neither reference, however, teaches that the composition comprises polyvinyl alcohols.

25. Frondoza teaches cell-containing implants comprising a variety of biodegradable polymers, such as those comprising poly(ethylene glycol) and polyvinyl alcohols (abstract; p. 5, par. 74). The reference teaches that the preparation of the implants can comprise photo-induced crosslinking (p. 5, par. 82) and that the method is advantageous because it requires no preformed scaffold and multiple formulation strategies for implantation (p. 5, par. 84). Since the formulation methods disclosed in Frondoza use the same components and techniques discussed in Liu, one of ordinary skill in the art would recognize that the biological matrices of Liu could be modified using the teachings of Frondoza to incorporate the additional components recited in the

method. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings to arrive at the claimed invention because Frondoza teaches that the matrices and multiple ingredients are compatible with a variety of cell types and Liu teaches that many types of polymers may be compatible with the cellular matrices taught therein. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

26. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM
/Ruth A. Davis/
Primary Examiner, Art Unit 1651